



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

JUN 29 2000

Date:

From: Acting Division Director, Division of Standards and Labeling Regulations, Office of Nutritional Products, Labeling, and Dietary Supplements, HFS-820

Subject: 75-Day Premarket Notification for New Dietary Ingredients

To: Dockets Management Branch, HFA- 305

New Dietary Ingredient: *Kalanchoe pinnata* (Lamarck) Persoon
Ruta Chalepensis L.

Firm: Isula Rain, Inc.
Date Received by FDA: April 19, 2000
90-Day Date: July 17, 2000

In accordance with the requirements of section 413(a) of the Federal Food, Drug, and Cosmetic Act, the attached 75-day premarket notification for the aforementioned new dietary ingredient should be placed on public display in docket number 95S-0316 after July 17, 2000.


Felicia B. Satchell

95S-0316

RPT 69



JUN 29 2000

Lawrence J. Brucia
President
Isula Rain, Incorporated
12 Skylark Drive, #31
Larkspur, California 94939

This is in response to your letter to the Food and Drug Administration (FDA) dated April 19, 2000, making a submission for new dietary ingredients pursuant to 21 U.S.C. 350b(a)(2) of the Federal Food, Drug, and Cosmetic Act (the Act)). Your letter notified FDA of the intent of Isula Rain, Inc. to market a product (Temporal Tension Extract) containing the new dietary ingredients *Kalanchoe pinnata* (Lamarck) Persoon and *Ruta chalepensis* L.

Under 21 U.S.C. 350b(a)(2), a manufacturer or distributor of a dietary supplement that contains a new dietary ingredient is required to submit to FDA, at least 75 days before the dietary ingredient is introduced or delivered for introduction into interstate commerce, information that is the basis on which the manufacturer or distributor has concluded that a dietary supplement containing such new dietary ingredients will reasonably be expected to be safe. FDA reviews this information to determine whether it provides an adequate basis for such a conclusion. Under section 350b(a)(2), there must be a history of use or other evidence of safety establishing that the dietary ingredient, when used under the conditions recommended or suggested in the labeling of the dietary supplement, will reasonably be expected to be safe. If this requirement is not met, the dietary supplement is deemed to be adulterated under 21 U.S.C. 342(f)(1)(B) because there is inadequate information to provide reasonable assurance that the new dietary ingredient does not present a significant or unreasonable risk of illness or injury.

FDA has carefully considered the information in your submission, and the agency has significant concerns about the evidence on which you rely to support your conclusion that the new dietary ingredients, *Kalanchoe pinnata* (Lamarck) Persoon and *Ruta chalepensis* L., will reasonably be expected to be safe. The information in your submission does not meet the requirements of 21 CFR 190.6(b)(3) because it does not contain a description of the dietary supplement that contains the new dietary ingredients including the level of the new dietary ingredients in the dietary supplement (see 21 CFR 190.6(b)(3)(i)), nor does it describe, in a quantitative manner, the amount to be consumed daily. The submission contains evidence of history of use and other information that you assert is an adequate basis to conclude that the dietary supplement containing the new dietary ingredients will reasonably be expected to be safe. However, the information in the submission is inadequate to make such a determination (see 21 CFR 190.6(b)(4)). Moreover, the submission provides no explanation or information that enables a determination to be

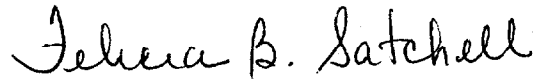
Page 2 – Mr. Lawrence J. Brucia

made that the citations in the submission are relevant to determining whether your product, as formulated and at the expected exposure when used as suggested in labeling, would reasonably be expected to be safe.

For the reasons discussed above, the information in your submission does not provide an adequate basis to conclude that *Kalanchoe pinnata* (Lamarck) Persoon and *Ruta chalepensis* L., when used under the conditions recommended or suggested in the labeling of your product, will reasonably be expected to be safe. Therefore, your product may be adulterated under 21 U.S.C. 342(f)(1)(B) as a dietary supplement that contain the new dietary ingredients specified for which there is inadequate information to provide reasonable assurance that such ingredients do not present a significant or unreasonable risk of illness or injury. Introduction of such products into interstate commerce is prohibited under 21 U.S.C. 331(a) and (v).

Please contact us if you have any questions concerning this matter.

Sincerely yours,

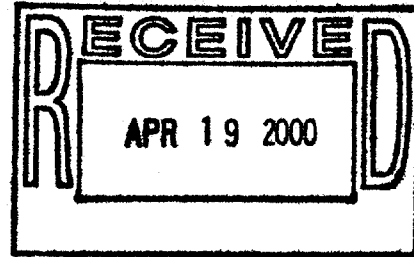
A handwritten signature in cursive script that reads "Felicia B. Satchell".

Felicia B. Satchell
(Acting) Division Director
Division of Standards
and Labeling Regulations
Office of Nutritional Products, Labeling
and Dietary Supplements

Isula RainTM inc.

April 11, 2000

Division of Food and Dietary Supplement Safety
Standards and Labeling
Office of Special Nutritionals
Center for Food Safety and Applied Nutrition
Food and Drug Administration
200 C Street, S.W. (HFS-450)
Washington, DC 20204



Dear Food and Drug Administration:

Pursuant to 21 CFR Section 190.6, requirement for premarket notification, Isula Rain Inc. wishes to notify the Food and Drug Administration that it will market the following list of herbs as dietary supplements:

Scientific Name

Common Name

Kalanchoe pinnata (Lamarck) Persoon
Ruta chalepensis L.

Q'ora Wayra
Ruta

These herbs will be distributed by Isula Rain Inc., 12 Skylark Drive, Unit 31, Larkspur, California 94939.

Attached please find a summary and reports which establish that these dietary ingredients, when used under ordinary recommended conditions, are reasonably expected to be safe. These reporting studies include:

- (1) The history of use or other evidence of safety establishing that the dietary ingredient will reasonably be expected to be safe.
- (2) Any citations to published articles and their reprints that support that the dietary ingredient will reasonably be expected to be safe.

Respectfully,

A handwritten signature in black ink, appearing to read "Lawrence J. Brucia", followed by a horizontal line.

Lawrence J. Brucia
President
Isula Rain, Inc.

70312

Review Number:2733
File Kalancho.pin
Reviewer/Date: pvb 4/27/00
Related Reviews:
Tracking:

BOTANICAL REVIEW

Common Names: qora wayra, air-plant

Latin Name: *Kalanchoe pinnata* (Lam.) Pers.

Synonym: *Bryophyllum calycinum* Salisb.

Botanical Family: Crassulaceae

Geographical Distribution:. Mexico, Madagascar, Mauritius

Related Species:

Food Use History:

Drug Use History: Leaves used in the healing or treating of
wounds. (Vulnerary)

Toxicity: None found.

Remarks:

References: KewCD 1993, Lyons 1907, RHSDG 1992

Review Number:2734
File Ruta.cha
Reviewer/Date: pvb 4/27/00
Related Reviews:
Tracking:

BOTANICAL REVIEW

Common Names: ruta, fringed rue

Latin Name: *Ruta chalapensis* Linn.

Synonym: *Ruta angustifolia* Pers.

Botanical Family: Rutaceae

Geographical Distribution:. Mediterranean

Related Species:

Food Use History:

Drug Use History: Juice of plant used for sore eyes and as
antihelmintic, emmenagogue, and abortive.

Toxicity: None found.

Remarks:

References: KewCD 1993

Kalanchoe pinnata

Scientific name: *Kalanchoe pinnata* (Lamarck) Persoon
(Common name: Q'ora Wayra, Coirama)

The botanical characteristics are described in the Analysis Certificate attached. (1) Ethnobotanical record is made of the internal use of this herb by South American populations (2,3,4,5,6).

The chemical composition of *Kalanchoe pinnata* through analysis includes alkaloids, flavonoids, tannins, steroid triterpenoids, and foam.

No ill-effects from its usage have been recorded.

1. Analysis Certificate, No. 939-98, La Molina Calidad Total Laboratorio, 1998
2. Duke, James A. and Vasquez, Rodolfo. Amazonian Ethnobotanical Dictionary. CRC Press, Boca Raton, Florida, 1994.
3. <http://www.rain-tree.com/coirama.htm>
4. Rosito Amgo, D.N. Rainforest Remedies. 2nd Revised Edition. 1993
5. Alfaro, Miguel A. Martinez. "Medicinal plants used in a totonac community of the sierra norte de puebla: tuzamapan de galeana, puebla, Mexico". Journal of Ethnopharmacology, 11, 1984.
6. Spring, Marline A. "Ethnopharmacologic analysis of medicinal plants used by laotian hmong refugees in minnesota". Journal of Ethnopharmacology, 26, 1989.

These documents appear in this order under "Literature"

Parts Used: leaves

Level

The level of *Kalanchoe pinnata* in the product "Temporal Tension Extract" (see below for entire ingredient listing) is

<u>Common name</u>	<u>Scientific name</u>	<u>Parts of the plant used</u>
Q'ora Wayra	<i>Kalanchoe pinnata</i> .	leaves
Ruda	<i>Ruta chalepensis</i>	Stem, leaves and flowers

Other ingredients: distilled water, ethyl alcohol derived from sugar cane

Condition of use:

The normal use recommended on the label of "Temporal Tension Extract" is:

Directions: Take one teaspoon mixed in a glass of hot or cold water as needed. Add honey if a sweetener is desired. If you'd like to avoid the consumption of alcohol, yet still enjoy the benefits of this product, add one teaspoon to a glass of hot, boiled water and let sit for 5 minutes. Do not exceed 4 teaspoons per day.

DO NOT USE THIS PRODUCT IF YOU ARE PREGNANT OR LACTATING

KEEP OUT OF THE REACH ON CHILDREN.

*Bryophyllum
pinnatum*

ANALYSIS CERTIFICATE

N° 939 - 98

CERTIFICATE OF VEGETABLE KIND

I DATA OF THE REQUESTING

Name : INTERNATIONAL CORPORATION
HEALTH AND LIFE E.I.R.L.
Address : Alfonso Cobian cooperative Mz.
H L I - Chacabayo

II DATA OF THE SERVICE

Service request : N° 1216 - 98
Date of service request : 98-09-08.
Requested service : Certificate of vegetable kind

III NAME OF THE PRODUCT : QORA HUAYRA

IV DATA OF THE SAMPLE

Size : 1 bag
Other characteristics : Containing folious stem

V USED LABORATORY : La Molina Calidad Total Laboratorio.

VI RESULTS

Of agreement to the Trial report Co- V- 165 - 98. that work in the files and reports the following:

The sample (stem folious) of "Qora Huayra", has been identified by orthodox method as: *Eulandia pinnata* L., which botanical classification according to A. Cronquist (1982) is:

KINGDOM	PLANTAE
DIVISION	MAGNOLIOPHYTA
CLASS	MAGNOLIOPSIDA
SUBCLASS	ROSIDAE
ORDER	ROSEPUSES
FAMILY	CRASSULACEAE
Genus	<i>Eulandia</i>
Species	<i>E. pinnata</i> .

METHOD USED IN THE LABORATORY

Classic method, orthodox According to A. Cronquist 1982

The certified present is referred exclusively to the analyzed sample, the one that is provided by the solicitor.
Any alteration or emendation nullifies the present document.
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October 9th, 1998 La Molina

ANALYSIS CERTIFICATE

N° 939 - 98

PHYTOCHEMIST TRIAL RUN CERTIFICATE

II. DATA OF THE REQUESTING

Name : INTERNATIONAL CORPORATION
HEALTH AND LIFE E.I.R.L.
Address : Alfonso Cobian cooperative Ma
H L I - Chacabayo

II. DATA OF THE SERVICE

Service request : N° 1216 - 98
Date of service request : 98-09-08
Requested service : Phytochemist trial run

III. NAME OF THE PRODUCT : QORAHUAYRA

IV. DATA OF THE SAMPLE

Size : 01 plant
Other characteristics : Containing folious stem

V. USED LABORATORY : SERVICIOS PROFESIONALES

VI. RESULTS

Of agreement to the Trial report N° 165- 98, that work in the files and reports the presence of the following components:

Alkaloids, flavonoids, tannin, steroids-triterpenoids, foam.

METHOD USED IN THE LABORATORY

Look de Ugaz Olga PHYTOCHEMIST investigation Method 1994

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October 9th, 1998 La Molina



EthnobotDB

Taxon : Kalanchoe pinnata

[PhytochemDB]

Family Crassulaceae

Genus Kalanchoe

Species pinnata

Species_author (LAM.) PERS.

Common_name Sedingin

Seringin

Other_info Ethnobotany Use Ache(Head) Kalanchoe pinnata Philippines

Asthma Kalanchoe pinnata Bahamas

Chest-Cold Kalanchoe pinnata Bahamas

Ear Kalanchoe pinnata Bahamas

Sore Kalanchoe pinnata Philippines

Strain Kalanchoe pinnata Bahamas

Fever Kalanchoe pinnata Malaya

Headache Kalanchoe pinnata Malaya

Select new class	Browse Taxon in EthnobotDB		View Taxon model	
Query by example	Query builder	ACeDB query language		Table maker
Select new DB				

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ROCKVILLE, MD 20852***

Ruta chalepensis

Scientific name: *Ruta chalepensis* L.
(Common name: Ruta)

The botanical characteristics are described in the Analysis Certificate attached. (1) Ethnobotanical record is made of the internal use of this herb by South American and North American Indians as well other populations around the world (1,2,3,4,5,6).

The chemical composition of *Ruta chalepensis* through analysis includes essence containing metilnonilcetone, metil-heptil cetone 90%, pineno, eucalyptus, metile solicilate, azuleno, glycosilated flavonoids, alkaloids, coumarins, chalepensisin, chalepin, and rutamarin.

No ill-effects from its usage have been recorded.

1. Analysis Certificate, No. 053-98, La Molina Calidad Total Laboratorio, 1998
2. Duke, James A. and Vasquez, Rodolfo. Amazonian Ethnobotanical Dictionary. CRC Press, Boca Raton, Florida, 1994.
3. Chevallier, Andrew. The Encyclopedia of Medicinal Plants. D.K Publishing Inc., NY, NY, 1996.
4. Plants for a future: database. <http://www.scs.leeds.ac.uk/cgi-bin/pfaf/arr>
5. Native American Ethnobotany Databse. <http://www.umd.umich.edu/cgi-bin/herb/>
6. de Feo, V. Medicinal and magical plants in the northern Peruvian Andes. Fitoterapia, Vol. 63, 1992.

These documents appear in this order under "Literature"

Parts used: leaves, stem, flower

s

Level

The level of *Ruta chalepensis* in the product "Temporal Tension Extract " (see below for entire ingredient listing) is

<u>Common name</u>	<u>Scientific name</u>	<u>Parts of the plants used</u>
Ruda	<i>Ruta chalepensis</i>	stem, leaves, flowers
Q'ora Wayra	<i>Kalanchoe pinnata</i>	leaves

Other ingredients: distilled water, ethyl alcohol derived from sugar cane.

Condition of use:

The normal use recommended on the label of "Temporal Tension Extract" is:

Directions: Take one teaspoon mixed in a glass of hot or cold water as needed. Add honey if a sweetener is desired. If you'd like to avoid the consumption of alcohol, yet still enjoy the benefits of this product, add one teaspoon to a glass of hot, boiled water and let sit for 5 minutes. Do not exceed 4 teaspoons per day.

DO NOT USE THIS PRODUCT IF YOU ARE PREGNANT OR LACTATING.

KEEP OUT OF THE REACH OF CHILDREN.

ANALYSIS CERTIFICATE
N° 053 - 98

CERTIFICATE OF VEGETABLE KIND

I. DATA OF THE REQUESTING

Name : INTERNATIONAL CORPORATION
HEALTH AND LIFE E.I.R.L.
Address : Alfonso Cobian cooperative Mz
H L I - Chacacayo

II. DATA OF THE SERVICE

Service request : Not 285 - 98
Date of service request : 98-05-06
Requested service : Vegetable kind

III. NAME OF THE PRODUCT

RUE

IV. DATA OF THE SAMPLE

Size : 50 g aprox
Other characteristics : Packed to bulk

V. USED LABORATORY

Professional services

VI. RESULTS

Of agreement to the Trial report No Co-V- 061 - 98 that work in the files the results are:

PHYSICAL DETERMINATION:

ASSAY	RESULTS
1. Specimen identification	Ruta chalepensis Family specie RUTACEAE

METHOD USED IN THE LABORATORY:

Classic method, orthodox.

VII. CONCLUSIONS :

Of agreement to the result obtained the sample from RUE corresponds to *Ruta chalepensis*.

-
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June 5th, 1998 La Molina

VI- MONOGRAPH OF THE VEGETABLE KIND: RUE

1. DESCRIPTION:

SUPRASPECIFIC CATEGORIES:

- KINGDOM	PLANTAE
- DIVISION	MAGNOLIOPHYTA
- CLASS	MAGNOLIOPSIDA
- SUBCLASS	ROSIDAE
- ORDER	SAPINDALES
- FAMILY	RUTACEAE
- Genus	<i>Ruta</i>
- Species	<i>R. chalepensis</i>

1.1 SCIENTIFIC NAME : *Ruta chalepensis*

1.2 SYNONYMY : Rue, fragrant rue.

1.3 BOTANICAL CHARACTERISTICS:

It is a perennial plant from 1 to 1,5 m heights. Its stem is herbaceous green color, very ramified, presents spherical prominents punctuations, it has not hair. Its leaves are alternate composite; it has a very disagreeable odor. Pedunculars flowers. tetrameras and pentameras.

It grows spontaneously or cultivated at coast, forest and jagged mountain range.

Root :	Underground, herbaceous, pivoltly, whitish yellow color.
Stem :	Aerial, erect, very ramified from its base, green bluish, cylindrical, up to 1 m height.
Leaves:	Alternate, peciolates, glaucous, composites, with seat folioles.
Flowers:	Cymose inflorescence, in umbel, little flowers, greenish yellow, calyx from 4 to 5 sepals, acute, corolla from 4 to 5 petals, slightly concave to the higher part.
Fruits :	Capsule, from 4 to 5 salient rugged lobes.

1.4 DISTRIBUTION :

Native from Europe. widely known in Peru.

2. COMMERCIAL SOURCE:

Leaves

3. CHEMICAL COMPOSITION:

It has essence-containing metilnonilcetone, metil-heptil cetone 90%, in addition to pineno, eucalyptus, metile solicilate, azuleno, and glycosilated flavonoids.

4. THERAPEUTIC PROPERTIES:

Antispasmodic (painful menstruation)

Used part : Leaves
Preparation: Infusion 5 g with 250 mL of hot water. Let it settle for 10 minutes.
Forms of use : Drink: drink a cup after meals.

Otitis:

Used part : Leaves
Preparation : Plaster. 10 g of crushed leaves.
Forms of use: Soaking a clean cotton with the plaster and put it to the hearing all night long.

Hearing pain and Headache

Used part : Leaves
Preparation : Fresh leaves
Ways of use: Soaking the fresh leaves in the head, temple and behind hearing.

5.

BIBLIOGRAPHY:

- "The plants cure", Alfonso Balbochas Publishing the present truth.
- "Guides of the medicinal plants ", Paul Schavenberg - Ferdinand Paris Publishing Omega S.A. Barcelona 1980 4th edition .
- "Catalogue of Medicinal Plants ", University of Lima Investigation center of the Industrial production CIPI 1944.
- Biologist Graciela Vilcapoma Segovia, according to A. Cronquist 1982.

Rinorea racemosa (Mart.) Ktze. Violaceae. "Yutubanco", "Limóncillo", "Cafecillo". Wood used in home construction. "Tirio" use the crushed bark of a Surinamese species for wasp stings (MJP).

Rollinia cardiantha Diels. Annonaceae. "Anona", "Anonilla". Fruit edible (RVM).

Rollinia curvipetala R.E.Fries. Annonaceae. "Anonilla". Fruit edible (RVM).

Rollinia cuspidata Mart. Annonaceae. "Anonilla". Fruit edible (RVM).

Rollinia edulis Pl. & Tr. Annonaceae. "Anona", "Anonilla". Fruit edible (RVM).

Rollinia mucosa (Jaq.) Baill. Annonaceae. "Anona". Cultivated. Fruit edible. (Fig. 202)

Rollinia pittieri Safford. Annonaceae. "Sacha anona". Wood used for house construction, beams, decks.

Rosa canina L. Rosaceae. "Rosa", "Rose". Cultivated. Ornamental.

Rosa centifolia L. Rosaceae. "Rosa del remedio", "Medicinal rose". Ornamental.

Rosa gallica L. Rosaceae. "Rosa". Cultivated. Ornamental.

Rosa indica L. Rosaceae. "Rosa Alejandrina", "Alexandran rose". Ornamental.

Roucheria punctata Ducke. Linaceae. "Puma caspi". Wood used for construction, beams, decks, and columns (RVM). "Taiwano" believe the bark decoction of the related *R. calophylla* Planch. is a "sure cure" for malaria (SAR).

Ruitzerania trichanthera (Spruce ex Warm.) Marcano-Berti. Vochysiaceae. "Quillo sisa", "Moena sin olor". Wood for lumber, general construction.

Ruizodendron ovale (R.&P.) R.E.Fr. Annonaceae. "Espintana". Wood is used for interior decoration.

Ruta chalepensis L. Rutaceae. "Ruda", "Rue". Cultivated. Around Iquitos, tied to many superstitions; a little branch of rue dispels bad spirits, and attracts clientele. Some merchants carry a rue leaf on their ears. Rue tea mixed with castor oil is well known as an oxytocic (SOU). Powdered leaves used to treat otitis, ophthalmia, and pediculosis. Leaf tea taken, perhaps dangerously, as antidysmenorrheic, antihysterical, cardiotonic, digestive, sedative, vermifuge. Vinegar decoction of leaves used for decongestant and sedative in myalgia (FEO). Brazilians use the tea for stroke (BDS). Psoralens in the plant may render photoTOXIC (JAD).

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